

Management of Small, Non-obstructing Renal Stones in Adults With Recurrent Urinary Tract Infections

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The management of small, non-obstructing renal stones in adults with recurrent lower urinary tract infections remains unclear. Whereas for larger or obstructing stones the decision to intervene becomes clearer, for stones smaller than 5 to 6 mm the decision to intervene requires consideration of multiple factors. This review describes these factors, including history, imaging, laboratory studies, as well as a comprehensive review of the literature. It remains of utmost importance that patients have additional possible etiologies appropriately evaluated and managed prior to intervention for their small renal stones.

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KEY WORDS

Non-obstructing renal stones • Recurrent urinary tract infections (rUTI)
• Percutaneous nephrolithotomy • Ureteroscopy • Shockwave lithotripsy

Patients with lower urinary tract infections (UTI) and non-obstructing renal calculi present a challenging clinical scenario. Recurrent UTIs (rUTI) are common across a large subset of patients. Their etiology, however, may vary by age and sex. In older women, for example, atrophic vaginitis secondary to estrogen deficiency contributes to a higher likelihood of UTIs. Older men may have elevated post-void residual volume secondary to bladder outlet obstruction, leading to persistent bacteriuria or even formation of bladder stones. Among all populations, however, the clinician must evaluate

for reversible causes of rUTIs that may serve as a foci of bacterial nidus, such as renal stones.¹

Among the general population, the detection of non-obstructing renal stones has increased as the utilization of cross-sectional imaging and sonography has increased.² In men, UTIs are generally classified as complicated, and, as such, warrant upper tract imaging.¹ In women, although the index patient with rUTI does not necessarily require imaging, those with complicated UTIs or particular risk factors, such as history of kidney stones or urease-splitting bacteria, should have upper tract imaging

performed. In a retrospective study by Wu and colleagues evaluating the yield of upper tract findings in 116 women with a history of rUTIs and trigonitis on cystoscopy, 6 of 116 (5%) had incidental small renal stones ranging from punctate to 3 mm, of which two-thirds had no prior stone history.³

Proteus, *Klebsiella*, *Pseudomonas*, or *Staphylococcus*, among others.⁵ In the general population, these infection stones may comprise up to 15% of all stone types. With elevated urine pH due to infection of the upper urinary tract, the patient becomes prone to formation of magnesium ammonium

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Barring absolute indications for renal stone intervention, the decision of whether to intervene on asymptomatic, small (≤ 5 mm) stones in patients with rUTIs requires consideration of multiple factors. Natural history studies have demonstrated that smaller stones are more likely to pass spontaneously, and are less likely to grow or become symptomatic compared with larger stones.⁴ According to the American Urological Association (AUA) guidelines, asymptomatic patients with non-obstructing renal stones may be closely observed as long as the patient is counseled and followed appropriately.² Treatment of these stones may become warranted in certain populations (eg, pilots, drivers) or in cases of associated symptoms, solitary renal units, ureteral obstruction, or when associated with infection. Whereas for larger or obstructing stones the decision to intervene becomes more straightforward, there have been limited series discussing the management of small renal stones with concomitant recurrent lower UTIs. This review discusses factors influencing the decision to treat small or low-burden non-obstructing renal stones in patients with rUTIs.

Infection and Infected Stones

Infection stones form secondary to urease-splitting organisms such as

phosphate (struvite) or calcium carbonate apatite stones. These stones grow crystals combined with bacteria and are often noted to be relatively porous and soft during lithotripsy. Antibiotics generally are impermeable to the depth of the stone, and it is not uncommon for the stone culture to be positive despite a negative voided urine culture.

Infected stones are any stone that is colonized with bacteria or yeast. All subtypes of kidney stones can be colonized, including infection stones.⁶ Whether the infection acts as a nidus, or whether the stone subsequently becomes colonized, remains unknown. Similarly to infection stones, antibiotics may not always penetrate the matrices of these stones, leading to bacterial persistence. Additionally, kidney stones may develop a bacterial biofilm like urinary catheters or ureteral stents.⁷ This impenetrable biofilm would additionally contribute to bacterial persistence that may contribute to the patient's lower UTIs.

There is a common notion that patients with bacterial persistence, defined as a rUTI with the same bacteria, should be evaluated for reversible causes of infection such as kidney stones or prostate infection.¹ Bacterial re-infection refers to a new infection with different organisms, and is believed to be due

to an ascending infection. Although the former situation of persistence is more commonly associated with infected stones, there is also the possibility that stones may contribute to bacterial reinfection with different organisms. The idea of upper tract exclusivity of bacterial colonization has been demonstrated in several series performing stone cultures (SC) at time of percutaneous nephrolithotomy (PCNL), with cultures being compared with pre-operative voided urine cultures and renal pelvis cultures.^{8,9} The discordance rate between SC and voided urine culture be as high as 35%. This suggests that the stone matrix or biofilm may support multiple organisms thriving in or on a renal stone, which may not be represented in a voided urine culture.

In cases of associated upper tract anomalies with concomitant small renal stones such as ureteropelvic junction obstruction or calyceal diverticulum, the physician must have a high degree of suspicion based upon history and imaging that the obstruction and urinary stasis may be contributing to a bacterial presence. Treating the obstruction as well as the stones may be prudent to reduce the likelihood of urinary stasis and associated bacterial colonization.

Imaging and Diagnostics

Cross-sectional imaging is limited with regards to the detection of infection stones. There is a wide variability in the Hounsfield units among struvite stones, making the definitive diagnosis challenging.¹⁰ Anecdotally, it has been observed that when using the bone window for viewing stones, a high-attenuation core with "soft" periphery may suggest an infection stone, or the converse of a "soft" core and encasing high-attenuating shell. Novel imaging modalities

such as dual-energy CT may aid in detection of uric acid stones, although more studies are required to improve the detection of non-uric acid and mixed stones.¹¹

Urine studies to suggest an infected renal calculus, short of removing and culturing the stone, are currently limited by their lack of specificity. Urine culture is important, as the presence of urease-splitting organisms may raise the degree of suspicion for an infection stone. Urinalysis may reveal an elevated urine pH, presence of leukocyte esterase, nitrites, or pyuria; however, these are unable to discern upper from lower tract infections.¹² The presence of coffin-shaped crystals are common with struvite stones, although are not commonly reported by all laboratories.¹³ Finally, selective upper tract irrigation and cultures may aid in localizing an upper tract bacterial source, although this is not commonly performed in routine clinical practice given the invasive nature of the procedure. There is likely more of a role for localization studies when a surgeon is contemplating nephrectomy in the setting of rUTIs with an atrophic, obstructed renal unit or a poorly functioning kidney in the setting of stones and infections or in bacteriuria where the source is not clear.

Treatment

In patients with rUTIs and small, non-obstructing renal stones, there are several medical options that should be considered prior to intervention on the stones. Behavioral modifications with copious hydration, timed voiding, and double voiding remain foundations for proper voiding practices. Clinicians may additionally advise patients to void before and/or after sexual

intercourse and are encouraged to discuss personal hygiene practices. Cranberry supplements may be offered to interested patients and are recommended to have greater than 36 mg of proanthocyanidins (PAC) to exert an impact on bacterial adhesion.¹⁴ Finally, there are a number of antibiotic regimens that may be offered including self-start therapy, post-coital prophylaxis, or daily prophylactic doses.¹ Use of these antibiotic regimens may carry greater risk of developing drug resistance or adverse effects related to the antibiotic. Additionally, the impact of prior antibiotic use on the gut and urinary microbiome and its subsequent role in the development of kidney stones is being increasingly demonstrated.¹⁵⁻¹⁷ In the era of greater antibiotic stewardship, clinicians must remain vigilant and adamant about prescribing antibiotics judiciously.

Surgical management of asymptomatic small or low-burden renal stones may be pursued when there is a high degree of suspicion that these may be contributing to lower UTIs, or in interested patients after risks and benefits are discussed. There are several published series addressing the question of managing renal stones in patients with lower UTIs. In the 2015 series by Omar and colleagues, 120 patients with a history of rUTIs who underwent treatment of their renal stones were evaluated.¹⁸ The preoperative mean stone size was 14 to 15 mm. All patients with residual fragments on postoperative imaging were excluded. Patients who did not develop postoperative UTIs were compared with those who did. The mean stone size among those who did not develop subsequent infections was 14 mm versus 15 mm in the group that did. Six percent of the group underwent ureteroscopy (URS), versus 61%

who had undergone PCNL and 33% who underwent shockwave lithotripsy (SWL). No difference in treatment type and the likelihood of infection was noted. Black patients and those with hypertension were more likely to have rUTIs. Patients with *Escherichia coli* UTIs were more likely to have resolved infections than those with preoperative *Enterococcus*. A more recent study by Agarwal and colleagues looked at the same question among 46 patients.¹⁹ Although patients with postoperative residual fragments were included in this series, patients with infection stones were excluded. The median stone burden was 20 mm (interquartile range, 14-35) and 70% had multiple stones. Forty-three percent of patients underwent URS versus 57% who underwent PCNL, and no difference was noted among the groups. Although 52% of the cohort had at least one UTI beyond the 30-day postoperative period, only 11% developed rUTIs using the commonly accepted rUTI definition. There was no difference in stone size between the two groups.

A major limitation of both series is the retrospective nature and selected inclusion criteria. Retrospectively evaluating post-surgical patients does not adequately address whether patients may have successful outcomes with medical management alone. In these studies, there is limited discussion of the medical management undertaken prior to surgical intervention, which is critical in these populations. The mean and median stones sizes in both cohorts were larger than 1 cm, without directly addressing outcomes in patients with smaller stones. Additionally, there are selection biases associated with what surgical treatment was undertaken, thereby

making further generalizability challenging.

When treating infection or infected stones, the surgeon should strive to render the patient stone-free, as their stone is presumably the nidus of infection. The surgeon may offer patients with asymptomatic stones either URS, SWL, or PCNL, depending upon the patient's anatomy, stone characteristics, and preferences. Perioperative antibiotics should be administered based upon culture data and in accordance with society guidelines. With regards to treatment modalities, PCNL has the advantage in that

of being more invasive. SWL, conversely, is the least invasive, but has the lowest SFR among the modalities.²⁰ There may be an additional bacteriostatic or even bactericidal benefit of SWL that has been demonstrated in several in vitro studies.²¹ URS for small renal stones is another option. The use of ureteral access sheaths may offer lower intrarenal pressures, and the holmium laser may similarly provide a bacteriostatic or bactericidal effect.^{22,23} In cases with stone specimen obtained, stone culture (aerobic and anaerobic) and analysis may be sent, when feasible.

consideration of how the rUTIs are managed prior to undergoing surgical intervention for stone disease. Prospective studies and randomized trials would provide much-needed evidence for guiding clinical management in these patients. There is additionally a deficiency in knowledge about the management of small, non-obstructing renal stones in patients with acute or chronic pyelonephritis.

Conclusions

Patients with rUTIs and small, non-obstructing renal calculi should be medically optimized prior to treating their renal stones. The optimal treatment method for infected or infection stones remains unknown, though clinicians should strive to achieve the highest stone-free rate when treatment is undertaken. Clinicians should remain judicious with their use of antibiotics, which should be used in accordance with society guidelines. ■

Additional research is needed to address deficiencies in the field with regards to the impact of small renal stones on rUTIs. Paramount to answering this question is the consideration of how the rUTIs are managed prior to undergoing surgical intervention for stone disease.

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MAIN POINTS

- According to the American Urological Association (AUA) guidelines, asymptomatic patients with non-obstructing renal stones may be closely observed as long as the patient is counseled and followed appropriately. Treatment of these stones may become warranted in certain populations (eg, pilots, drivers) or in cases of associated symptoms, solitary renal units, ureteral obstruction, or when associated with infection.
- In the general population, infection stones may comprise up to 15% of all stone types. Infected stones are any stone that is colonized with bacteria or yeast. All subtypes of kidney stones can be colonized, including infection stones. Antibiotics may not always penetrate the matrices of these stones, leading to bacterial persistence. Additionally, kidney stones may develop a bacterial biofilm like urinary catheters or ureteral stents. This impenetrable biofilm would also contribute to the bacterial persistence that may cause the patient's lower UTIs.
- Novel imaging modalities such as dual-energy CT may aid in detection of uric acid stones, although more studies are required to improve the detection of non-uric acid and mixed stones.
- Medical options that should be considered prior to intervention include behavioral modification and carefully considered antibiotic regimens. Surgical management of asymptomatic small or low-burden renal stones may be pursued when there is a high degree of suspicion that these may be contributing to lower UTIs, or in interested patients after risks and benefits are discussed.

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